Research Article

Regulation mechanism of heartbeat rate, shocked blood volume, and their formation heterochronousity among small laboratory animals

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ABSTRACT

Objective: The purpose of this study was to study the peculiarities of HR, SVB, and the mechanisms of their regulation development among rats from the 1st day of life and up to the age of 70 days. **Methods:** The method of tetrapolar thoracic rheography was used to determine the HR and shock volume of blood (SVB). The principle of impedance electroplethysmography method is to record the oscillations of the complex electrical resistance (impedance) of a bioobject for high-frequency current; the fluctuations of resistance are proportional to the changes in blood supply. **Results:** In experiments on white mongrel laboratory rats, it was established that from the 1st day of life to the age of 70 days, the periods of the greatest change in the heart rate of rats alternate with the stages of a significant increase in the shock volume of the blood. In the mechanisms of regulation of the shock volume of blood in rats, the sympathetic regulatory effect is manifested much earlier than the parasympathetic. **Conclusion:** However, in the future, their ratio changes somewhat: A more pronounced sympathetic regulatory effect on UCS persists up to 70 days of age, whereas from the 8-week-old age, the parasympathetic effect is significantly reduced.

KEY WORDS: Heart rate, Heterochronicity, M-cholinoblocker, Stroke volume, α-Blocker

INTRODUCTION

The mechanisms of heart pumping function regulation are studied by most researchers under the conditions of model experiments on animals.[1-4] A significant number of studies is devoted to the heart rate (HR) regulation mechanisms in a developing organism. They studied the changes of HR and stroke volume of blood (SVB) in a developing organism via. Shock volume of blood (SVB) in a developing organism via.[5-8] Numerous studies are devoted to the study of heart functions in various physiological situations. Motor activity is an important factor of heart functional improvement in ontogenesis.

However, the obtained data are fragmentary, and there is no holistic view on the peculiarities of HR and stroke volume of blood development. A significant number of works is also devoted to the study of mechanism development regularities for heart regulation in a developing organism.[9-12] At that, the dependence of heart chronotropic function on the sympathetic and parasympathetic system was studied in more detail. However, up to now, the researchers have no common opinion on the development of mechanisms for the regulation of heart chronotropic function in a developing organism. Moreover, the features of the sympathetic and parasympathetic parts of the autonomic nervous system development during the regulation of the shock volume of blood in a developing organism remain almost unexplored.[13,14]

The purpose of this study was to study the peculiarities of HR, SVB, and the mechanisms of their regulation development among rats from the 1st day of life and up to the age of 70 days.

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METHODS OF RESEARCH

The method of tetrapolar thoracic rheography was used to determine the HR and shock volume of blood (SVB). The principle of impedance electroplethysmography method is to record the oscillations of the complex electrical resistance (impedance) of a bioobject for high-frequency current; the fluctuations of resistance are proportional to the changes in blood supply. These changes in resistance enhanced by electronic devices and recorded graphically form a curve called rheogram (flow).

The method has a number of undeniable advantages: Non-invasiveness and promptness, continuity and any duration of observation, technical simplicity and absolute atraumaticity, and the possibility of measurements at free breathing.[15]

Thoracic tetrapolar rheography was used as a basic medical technique in the complex "Reodyne-500." The developed algorithm for the automatic evaluation of hemodynamic parameters allows to localize all phase structures of the bioimpedance signal without operator intervention. The necessary reference points of the signal (the beginning of the systolic and diastolic waves, the end of the expulsion period, the maxima of the systolic and diastolic waves, and the end of the expulsion period) change with an error of no >1.0% relative to a highly qualified expert markup.

The differentiated rheogram was recorded among the rats with administered sodium pentobarbital (40 mg/kg) and natural respiration using "RPG-204" device. To study the sympathetic effects on the pump function of the rat heart, 0.1% obsidian solution was injected into the jugular vein through the catheter at a dose of 0.8 ml/100 g. 0.1% solution of atropine sulfate was injected to block the parasympathetic effects. The severity of sympathetic and parasympathetic influences on the pumping function of the rat heart was assessed by the shifts of HR and SBV after the pharmacological blockade of the corresponding receptors.

Table 1: The changes of HR and SVB among rats, from birth to 70 days of age

Age (days)	*n* (am)	HR (beats/min)	SVB (ml)
1	8	303.67±15.1	0.012±0.006
7	9	351.7±17.3*	0.03±0.006
14	9	380.9±19.3	0.045±0.007*
21	8	459.7±17.7*	0.052±0.007
28	8	471.5±19.3	0.069±0.009*
35	13	470.1±13.5	0.091±0.009
42	14	438.77±11.8	0.121±0.011*
49	11	429.1±15.5	0.142±0.009
56	12	414.1±14.1	0.165±0.007*
63	11	418.5±14.8	0.201±0.007*
70	14	417.39±14.1	0.221±0.008

*Reliability of changes as compared to previous age (P<0.05). HR: Heart rate

STUDY RESULTS AND THEIR DISCUSSION

In the process of rat natural growth and development, the HR does not change unidirectionally. Thus, during the first 5 weeks of animal life, there is a persistent increase of the HR [Table 1]. It should be noted that the rate of increase in HR is not the same. A significant increase in HR in rats is observed at 1–3 weeks of life, where the HR increase was 48.1 ± 7.8 and 65.4 ± 8.9 bpm, respectively ($P < 0.05$). At the 2nd and the 4th week of life, the HR increase among rats was less pronounced and amounted to only 24.6 ± 7.6 and 9.2 ± 7.7 beats/min. Consequently, ring the first 5 weeks of life, the periods of a significant HR increase among rats, alternate with the stages of less pronounced HR changes. Later, starting from the 6th week of rat life and up to the 10th week of age, a steady decrease of the HR was observed.

The shock volume of blood increases among the rats from the 1st day of life and up to the age of 70 days. At the same time, the rates of systolic ejection growth are not the same. A significant increase of SVB among animals was observed only at the 2nd, 4th, 6th, 8th, and 9th weeks of life by 0.012 ± 0.005, 0.018 ± 0.007, 0.026 ± 0.004, 0.026 ± 0.005, and 0.033 ± 0.007 ml ($P < 0.05$), respectively. Thus, there is a significant increase of SVB after every 2 weeks of animal life.

The comparative analysis of HR and SVB changes among rats, from the 1st day of life and up to the age of 70 days, indicates that the periods of the greatest HR change alternate with the stages of the shock volume of blood significant increase. Consequently, it can be argued that the HR and the shock volume of blood among rats vary at different times, i.e., heterochronically.

The introduction of α-adrenoreceptor blocker - obsidian not at all stages of animal life led to a significant reduction of HR [Table 2]. A significant decrease of HR for the administration of obsidian was observed only at the 10-day age, where the HR response was 39.4 ± 11.4 beats/min ($P < 0.05$). Subsequently, before the 5th week of life, the response of the HR to the administration of obsidian increased. However, it became unreliable again from the 6th week of age. This indicates that the sympathetic regulatory effect on HR is reliably manifested at the end of the 2nd week of rat life. In the future, its influence is greatly enhanced and reaches its maximum values by the 4th week of age. However, among 6-week-old rats, the influence of the autonomic nervous system sympathetic department on the HR is significantly reduced. The introduction of M-cholinoblocker - atropine caused a significant increase of HR by 20.4 ± 6.4 bpm among 6-day-old

Table 2: Response of HR and SVB to administration of obsidan and atropine

Days	*n*	Original		After the introduction of obsidan		After the introduction of atropine	
		HR	SVB	HR	SVB	HR	SVB
1	8	303.6±15.1	0.012±0.003	293.9±12.4	0.008±0.001	316.0±8.1	0.014±0.005
7	9	351.7±17.3	0.031±0.006	336.1±12.6	00006±0.006*	371.2±8.2*	0.035±0.008
14	9	380.9±19.3	0.045±0.007	327.5±13.8*	0.016±0.003*	402.3±8.4*	0.067±0.007*
21	8	459.7±17.7	0.052±0.007	393.9±13.1*	0.019±0.002*	471.0±8.7*	0.079±0.007*
28	8	471.5±19.3	0.069±0.009	385.8±12.8*	0.037±0.007*	495.4±8.8*	0.099±0.009*
35	13	470.1±13.5	0.091±0.009	429.0±13.1*	0.058±0.007*	495.3±8.9*	0.129±0.014*
42	14	438.7±11.8	0.121±0.011	403.6±11.8*	0.083±0.007*	474.1±9.2*	0.165±0.017*
49	11	429.1±13.1	0.142±0.009	390.9±11.3*	0.104±0.006*	459.5±9.0*	0.188±0.018*
56	12	414.1±14.1	0.165±0.007	398.7±11.5	0.129±0.008*	436.6±9.1	0.207±0.018
63	11	418.5±14.8	0.201±0.007	403.8±12.8	0.171±0.009*	443.8±9.2	0.241±0.02
70	14	417.3±14.1	0.221±0.008	399.6±13.3	0.191±0.01*	436.2±8.8	0.258±0.02

*Reliability of changes as compared to original data (P<0.05). HR: Heart rate

ones (P < 0.05). Subsequently, before the 6-week-old age, the response of the HR to the administration of atropine increased, and then, it decreased significantly. Consequently, the parasympathetic regulatory effect on HR begins to appear at the end of 1 week of animal life and increases up to 6 weeks of age. However, then, its influence on HR weakens and becomes not authentic at the age of 43 days. Thus, the parasympathetic regulatory effect on HR begins to manifest significantly earlier than the sympathetic one. However, there is the decrease in sympathetic and parasympathetic regulatory effect on HR among the 6-week-old rats, i.e. ,the desire of the body to self-regulation is observed.

The sympathetic influence manifests itself much earlier than the parasympathetic effect in the regulation of the shock volume of blood. Thus, after the introduction of obsidian, the SVB decreased significantly by 0.010 ± 0.002 ml (P < 0.05) at the 4 days of age. Consequently, the sympathetic regulatory effect on SVB begins to appear already in the middle of 1 week of rat life and with some changes increase to 7 weeks of age. Subsequently, there is a certain tendency to decrease the sympathetic regulatory effect on the shock volume of blood. A significant increase of the shock volume of blood after the administration of M-choline blocker - atropine was first recorded in the 14-day-old age. Consequently, the parasympathetic regulatory effect on SVB began to appear only by the end of the 2nd week of rat life. Later, its influence gradually increases and reaches its maximum value by the age of 7 weeks. The reaction of SVB on the administration of atropine at the age of 49 days was 0.048 ± 0.009 ml (P < 0.05). However, then, the parasympathetic regulatory effect on SVB began to weaken and starting from the 8th week of rat life; the reaction of SVB to atropine was not reliable. Thus, in the regulation of the shock volume of blood, the sympathetic regulatory effect is manifested much earlier than the parasympathetic one. Further, during the 2nd and the 3rd weeks of the animal life, the sympathetic and parasympathetic regulatory effect on the SVB is expressed approximately equally. However, in the future, their ratio slightly changes: A more pronounced sympathetic regulatory effect on SVB persists up to the age of 70 days, whereas since the age of 8 weeks the parasympathetic effect is significantly reduced.

CONCLUSIONS

1. During the first 5 weeks of life, there is a significant increase of HR among rats. Later, a steady decrease in the HR was observed starting from the 6th week of rat life to the 10th week of age.
2. In the process of animal natural growth and development, a significant increase of cardiovascular activity occurs every 2 weeks of rat life.
3. The parasympathetic regulatory effect on HR of rats begins to manifest significantly earlier than sympathetic one. However, from the 6-week-old age, there is the decrease in sympathetic and parasympathetic regulatory effect on rat HR.
4. During the regulation of the shock volume of the blood, the sympathetic regulatory effect is manifested much earlier than the parasympathetic one.

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REFERENCES

1. Sitdikov FG. A Developing Heart and an Impellent Mode. Kazan: Disease from the Candan of Biologic Sciences; 1998. p. 95.
2. Gilmutdinova RI, Anikina TA. The influence of Physical Loads on Cholinergic Regulation of Heart. Problems of Adaptation to Muscular Loads. Kazan: Disease from the Candan of Biologic Sciences; 1995. p. 68.
3. Zefirov TL, Svyatova NV. Auto-nomic control of cardiac function involves modulation of hy-perpolarization activated channels *in vitro*. Bull Expert Biol 1998;126:612-4..
4. Kulaev BS, Antsiferova LI. Ontogenesis of the Autonomic Nervous System. Physiology of the Autonomic Nervous System: The Guide to Physiology L.; 1981. p. 495-511.
5. Nigmatullina RR, Abzalov RA, Sitdikov FG. The effect of

extracardiac nerve blockade on the shock volume of blood in postnatal ontogenesis among rats. Physiol J 1992;7:965-9.
6. Tikhonova OA. Peculiarities of the Rat Heart pump function during the Transition from Hypokinesia to other Motor Regimes. Kazan: Dis from the Cand. of Biol. Sciences; 2003.
7. Kubicek WG, Kamegis JW, Patterson RP, Witsoe DA, Mattson RH. Development and evaluation of an impedance cardiac output system. Aerosp Med 1996;37:1208-12.
8. Baker DG, Don HF, Brown JK. Alpha-adrenergic and muscarinic cholinergic inhibition of ACh release in guinea pig trachea: Role of neuronal K+ channels. Am J Physiol 1994;266:L698-704.
9. Cooke L, Muntz KH. Differences in beta adrenergic receptor agonist affinity between cardiac myocytes and coronary arterioles in canine heart. J Pharmacol Exp Ther 1994;269:351-7.
10. Degoute CS, Preckel MP, Dubreuil C, Banssillon V, Duclaux R. Sympathetic nerve regulation of cochlear blood flow during increases in blood pressure in humans. Eur J Appl Physiol Occup Physiol 1997;75:326-32.
11. Gajek J, Zysko D. The influence of the tilt training program on sympathetic nervous system activity to the head-up tilt test. Eur Heart J 2003;24:272.
12. Middeke M, Reder S, Holzgreve H. Regulation of the beta-adrenoceptor-cAMP-system during dynamic exercise in patients with primary hypertension after acute beta-blockade. Blood Press 1994;3:189-92.
13. Nakamura I, Yamamoto Y, Muraoka I. Autonomic control of heart rate during physical exercise and fractal dimension of heart rate variability. J Appl Physiol 1993;74:875-81.
14. Niess A, Roecker K, Mayer F, Heitkamp HC, Dickhuth HH. Effect of combined parasympathetic and sympathetic blockade on left ventricular relaxation at rest and during exercise in trained and untrained men. Int J Sports Med 1996;17 Suppl 3:S180-3.
15. Sh ME. The role of α1 and β-Adrenergic Receptors in the Regulation of Cardiac Output of a Growing Organism. Kazan: Author's Abstract from the Diss. by the Cand. of Biol. Sciences; 1997. p. 16.

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